09/937966
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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
United States of America

in its capacity as elected Office

Date of mailing (day/month/year) 19 December 2002 (19.12.02)	
International application No. PCT/US01/27605	**Applicant's or agent's file reference** 650053.91533
International filing date (day/month/year) 06 September 2001 (06.09.01)	**Priority date** (day/month/year) 03 November 2000 (03.11.00)
Applicant ROMAN, Richard, J. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

07 May 2002 (07.05.02)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Olivia TEFY
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Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/036108 A3

(54) Title: USE OF 20-HETE SYNTHESIZING ENZYME INHIBITORS AS THERAPY FOR CEREBRAL VASCULAR DISEASES

(57) Abstract: A method for treating cerebral vascular diseases in a human or non-human animal is disclosed. The method involves inhibiting 20-HETE synthesizing enzyme activity sufficiently to increase or prevent a decrease in cerebral blood flow in the human or non-human animal. This can be obtained by treating the animal with inhibitors of CYP4A or CYP4F family of enzymes, such as HET0016, 17-ODYA (17-octadecynoic acid), DDMS (dibromododecenyl methylsulfimide), 1-ABT (1-aminobenzotriazole) and miconazole, or with an antibody to 20-HETE synthetizing enzyme or with an antisense oligo-nucleotide directed against 5' end of CYP4A1, CYP4A2, CYP4A11, CYP4F2 or CYP4F3.

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44) 9937946

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
650053.91533		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 01/ 27605	06/09/2001	03/11/2000
Applicant		
MCW RESEARCH FOUNDATION, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. NONE

   [ ] as suggested by the applicant.

   [X] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

[redacted]tional application No.
PCT/US 01/27605

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

A method for treating cerebral vascular diseases in a human or non-human animal is disclosed.The method involves inhibiting 20-HETE synthesizing enzyme activity sufficiently to increase or prevent a decrease in cerebral blood flow in the human or non-human animal. This can be obtained by treating the animal with inhibitors of CYP4A or CYP4F family of enzymes, such as HET0016, 17-ODYA (17- octadecynoic acid), DDMS (dibromododecenyl methylsulfimide), 1-ABT (1-aminobenzotriazole) and miconazole, or with an antibody to 20-HETE synthetizing enzyme or with an antisense oligo-nucleotide directed aginst 5' end of CYP4A1, CYP4A2, CYP4A11, CYP4F2 or CYP4F3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/[redacted]01/27605

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/155 A61K31/145 A61K31/20 A61K31/4192 A61K31/4174
A61K39/395 A61K48/00 A61P9/10 A61P31/00 A61P25/00
A61P25/06 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, PASCAL, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 01 32164 A (AMADA HIDEAKI ;ISHII TAKAAKI (JP); SATO MASAKAZU (JP); KOBAYASHI Y) 10 May 2001 (2001-05-10) abstract ---	1,2
Y	WO 99 43310 A (MCW RES FOUND INC) 2 September 1999 (1999-09-02) page 4, line 22 -page 5, line 4 page 12, line 11 - line 17 page 59, line 6 - line 8 page 60, line 24 -page 61, line 3 claim 18 --- -/--	1-34

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 July 2002	12/08/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Villa Riva, A

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSI[redacted]ED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	LANGE ET AL: "20-HETE-induced vasoconstriction and inhibition of potassium current in cerebral vascular smooth muscle is dependent on activation of protein kinase C" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 272, no. 43, 24 October 1997 (1997-10-24), pages 27345-27352, XP002111652 ISSN: 0021-9258 page 27345, left-hand column, line 6 -right-hand column, line 1 page 27345, right-hand column, line 28 - line 30 figure 1 page 27351, right-hand column, last paragraph	1-34
Y	HARDER DAVID R ET AL: "Formation and action of a P-450 4A metabolite of arachidonic acid in cat cerebral microvessels." AMERICAN JOURNAL OF PHYSIOLOGY, vol. 266, no. 5 PART 2, 1994, pages H2098-H2107, XP001094418 ISSN: 0002-9513 abstract page H2098, right-hand column, line 39 - line 45 page H2106, right-hand column, last paragraph	1-34
Y	ZOU AI-PING ET AL: "Inhibition of renal vascular 20-HETE production impairs autoregulation of renal blood flow." AMERICAN JOURNAL OF PHYSIOLOGY, vol. 266, no. 2 PART 2, 1994, pages F275-F282, XP001094419 ISSN: 0002-9513 the whole document	1-34
P,A	MIYATA N ET AL: "HET0016, a potent and selective inhibitor of 20-HETE synthesizing enzyme." BRITISH JOURNAL OF PHARMACOLOGY. ENGLAND JUN 2001, vol. 133, no. 3, June 2001 (2001-06), pages 325-329, XP001094460 ISSN: 0007-1188 abstract; figures page 328, right-hand column, last paragraph	1-34

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/[redacted]01/27605

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			CN	1291890 T	18-04-2001
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			US	2002049244 A1	25-04-2002
			US	2002072534 A1	13-06-2002
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			US	6395781 B1	28-05-2002